

37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 50-0622.

AMENDMENT

In the Specification:

Please put a period after the text in lines 10 and 11 on page 130 as follows:

- (g) Incubate at 4°C (hold).
- (h) END.

Please put a period after the text in line 22 on page 134 as follows:

- (ii) 30 cycles of 92°C denaturation for 15 sec; 60°C primer annealing for 20 sec; and 72°C primer extension for 40 sec.

Please put a period after the text in line 30 on page 140 as follows:

35) After binding collect SA-PMPs through use of a magnet and recover flow through material (SAVE THIS MATERIAL!).

On page 17, please replace the paragraph in lines 10-19 with the following paragraph:

① **FIG. 1.** Schematic diagram of gene activation events described herein. The activation construct is transfected into cells and allowed to integrate into the host cell chromosomes at DNA breaks. If breakage occurs upstream of a gene of interest (e.g., Epo), and the appropriate activation construct integrates at the break such that its regulatory sequence becomes operably linked to the gene of interest, activation of the gene will occur. Transcription and splicing produce a chimeric RNA molecule containing exonic sequences from the activation construct and from the endogenous gene. Subsequent translation will result in the production of the protein of interest. Following

isolation of the recombinant cell, gene expression can be further enhanced via gene
amplification. The polyA tail is set forth in SEQ ID NO:33.

On page 21, please replace the paragraph in lines 6-17 with the following
paragraph:

FIG. 13. Illustration depicting two transcripts produced from the integrated vectors described in Figures 12A-12G. DNA strands are depicted as horizontal lines. Vector DNA is shown as a black line. Endogenous genomic DNA is shown as a grey line. Rectangles depict exons. Vector-encoded exons are shown as open rectangles, while endogenous exons are shown as shaded boxes. S/D denotes a splice donor site. Following integration, the vector encoded promoters activate transcription of the endogenous gene. Transcription resulting from the upstream promoter produces a spliced RNA molecule containing the vector encoded exon joined to the second and subsequent exons from an endogenous gene. Transcription from the downstream promoter, on the other hand, produces a transcript containing the sequences downstream of the integrated DNA joined to exon I and the subsequent exons from an endogenous gene. The polyA tails are set forth in SEQ ID NO:33.

On page 26, please replace the paragraph in lines 6-25 with the following
paragraph:

FIG. 23A-23D. Example of a multi-Promoter/Activation Exon Vector. Each vector is illustrated schematically in its linearized form. Each horizontal line represents a DNA molecule. The arrows denote promoter sequences. Boxes indicate exons. Hatched boxes indicate untranslated regions. It is understood that the exons on these vectors may

be untranslated, or may contain a start codon and additional codons as described herein.

The following designations were used: splice donor site (S/D), vector promoter #1 (VP #1), vector promoter #2 (VP #2), vector promoter #3 (VP #3), and vector promoter #4 (VP #4). Individual vector activation exons are designated A, B, C, and D (SEQ ID NOS: 29-32, respectively). Each activation exon may contain a different structure. The structure of each activation exon and its flanking intron are shown below. It is understood, however, that any activation exon described herein, may be used on these vectors, in any combination and/or order, including exons that encode signal sequences, partial signal sequences, epitope tags, proteins, portions of proteins, and protein motifs.

D3
Any of the exons may lack a start codon. In addition, while not illustrated in these examples, these vectors may contain a selectable marker and/or an amplifiable marker. The selectable marker may contain a poly (A) signal or a splice donor site. When present, the splice donor site may be located upstream or downstream of the selectable marker. Alternatively, the selectable marker may not be operably linked to a poly (A) signal and/or a splice donor site.

On page 29, beginning at line 19, please replace lines 19-25 with the following

lines:

D4
FIG. 29A-29B. Nucleotide sequence of pRIG14. (SEQ ID NO: 21).

FIG. 30A-30C. Nucleotide sequence of pRIG19. (SEQ ID NO.: 22).

FIG. 31A-31C. Nucleotide sequence of pRIG20. (SEQ ID NO.: 23).

FIG. 32A-32C. Nucleotide sequence of pRIGad1. (SEQ ID NO.: 24).

FIG. 33A-33D. Nucleotide sequence of pRIGbd1. (SEQ ID NO.: 25).

FIG. 34A-34B. Nucleotide sequence of pUniBAC. (SEQ ID NO.: 26).